# Sequence Listing 10/519390 Sequence Listing

<110>	MEDEXGEN Inc. CHUNG, Yong-Hoon LEE, Hak-sup YI, Ki-Wan HEO, Youn-Hwa KIM, Jae-Youn
<120>	A method of improving efficacy of biological response-modifying proteins and the exemplary muteins
<150>	KR10-2003-0051846
<151>	2003-07-26
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	replaced by Val.
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	Phe Thr Glu His Ser Pro Leu Thr Pro His Arg Arg Asp Leu
1	5 10 . 15
cys ser	Arg Ser Ile Trp Leu Ala Arg Lys Ile Arg Ser Asp Leu Thr
	20 25 30
Ala Tau	Mha Clu Cau Man Val I a Win Cl
Ara reu	Thr Glu Ser Tyr Val Lys His Gln Gly Leu Asn Lys Asn Ile
	35 40 45
Asp to-	Ann Con Ale Den Clu Mat Dre Vel Ti Commission -
	Asp Ser Ala Asp Gly Met Pro Val Ala Ser Thr Asp Gln Trp
50	. 55 60

Ser Glu Leu Thr Glu Ala Glu Arg Leu Gln Glu Asn Leu Gln Ala Tyr Arg Thr Phe His Val Leu Leu Ala Arg Leu Leu Glu Asp Gln Gln Val 90 His Phe Thr Pro Thr Glu Gly Asp Phe His Gln Ala Ile His Thr Leu 105 Leu Leu Gln Val Ala Ala Phe Ala Tyr Gln Ile Glu Glu Leu Met Ile 120 Leu Leu Glu Tyr Lys Ile Pro Arg Asn Glu Ala Asp Gly Met Pro Ile 135 Asn Val Gly Asp Gly Gly Leu Phe Glu Lys Lys Leu Trp Gly Leu Lys 150 155 Val Leu Gln Glu Leu Ser Gln Trp Thr Val Arg Ser Ile His Asp Leu 165 170 Arg Phe Ile Ser Ser His Gln Thr Gly Ile Pro Ala Arg Gly Ser His 180 185 Tyr Ile Ala Asn Asn Lys Lys Met 195 200 <210> 2 <211> 166 <212> <213> Artificial Sequence <220> <223> EPO: 48th, 138th, 142nd or 148th Phe is replcaced by Val. <400> Ala Pro Pro Arg Leu Ile Cys Asp Ser Arg Val Leu Glu Arg Tyr Leu 10

Cys	Ser	Leu 35	Asn	Glu	Asn	Ile	Thr 40	Val	Pro	Asp	Thr	Lys 45	Val	Asn	Phe	
Tyr	Ala 50	Trp	Lys	Arg	Met	Glu 55	Val	Gly	Gln	Gln	Ala 60	Val	Glu	Val	Trp	
Gln 65	Gly	Leu	Ala	Leu	Leu 70	Ser	Glu	Ala	Val	Leu 75	Arg	Gly	Gln	Ala	Leu 80	
Leu	Val	Asn	Ser	Ser 85	Gln	Pro	Trp	Glu	Pro 90	Leu	Gln	Leu	His	Val 95	Asp	
Lys	Ala	Val	Ser 100	Gly	Leu	Arg	Ser	Leu 105	Thr	Thr	Leu	Leu	Arg 110	Ala	Leu	
Arg	Ala	Gln 115	Lys	Glu	Ala	Ile	Ser 120	Pro	Pro	Asp	Ala	Ala 125	Ser	Ala	Ala	
Pro	Leu 130	Arg	Thr	Ile	Thr	Ala 135	Asp	Thr	Phe	Arg	Lys 140	Leu	Phe	Arg	Val	
Tyr 145	Ser	Asn	Phe	Leu	Arg 150	Gly	Lys	Leu	Lys	Leu 155	Tyr	Thr	Gly	Glu	Ala 160	
Cys	Arg	Thr	Gly	Asp 165	Arg											
<210		3														
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<212 <213		PRI Art		cial	Sequ	ence	<b>!</b>									
<220	)>															
<223	3>	Flt Val		6th,	15t	h, 8	lst,	87t	h, 9	6th	or 1	.24th	Phe	is	replaced	ру

Leu Glu Ala Lys Glu Ala Glu Asn Ile Thr Thr Gly Cys Ala Glu His

20

<400	)>	3													
Thr	Gln	Asp	Cys	Ser	Phe	Gln	His	Ser	Pro	Ile	Ser	Ser	Asp	Phe	Ala
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Val	Lys	Ile	Arg	Glu	Leu	Ser	Asp	Tyr	Leu	Leu	Gln	Asp	Tyr	Pro	Val
			20					25					30		
Thr	Val	Ala	Ser	Asn	Leu	Gln	Asp	Glu	Glu	Leu	Cys	Gly	Gly	Leu	Trp
		35					40					45			
Arg	Leu	Val	Leu	Ala	Gln	Arg	Trp	Met	Glu	Arg	Leu	Lys	Thr	Val	Ala
	50					55					60				
Gly	Ser	Lys	Met	Gln	Gly	Leu	Leu	Glu	Arg	Val	Asn	Thr	Glu	Ile	His
65					70					75					80
Phe	Val	Thr	Lys	_	Ala	Phe	Gln	Pro		Pro	Ser	Cys	Leu	-	Phe
				85					90					95	
			_			_			<b>63</b> -	<b>61</b>	m1	<b>.</b>	<b>61</b>	G1	•
Val	GIn	Thr		Пе	Ser	Arg	Leu		Gin	Glu	Thr	Ser		GIn	Leu
			100					105					110		
77 - 7	71.	T 011	T	Dro	T mm	Tlo	Πρ∾	7 ~~	Cln	7 cn	Pho	202	7 20	Cvc	LOU
vaı	АТА		гуѕ	PIO	пр	116	120	Arg	GIII	Asn	rne	125	Arg	Cys	Leu
		115					120					125			
Glu	T.e.11	Gln	Cvs	Gln	Pro	Asp	Ser	Ser	Thr	Leu	Pro	Pro	Pro	Trp	Ser
	.130	Q1	Cyb	02		135	501	001			140				
Pro	Arg	Pro	Leu	Glu	Ala	Thr	Ala	Pro	Thr	Ala	Pro	Gln	Pro	Pro	Leu
145					150					155					160
Leu	Leu	Leu	Leu	Leu	Leu	Pro	Val	Gly	Leu	Leu	Leu	Leu	Ala	Ala	Ala
				165					170					175	
Trp	Cys	Leu	His	Trp	Gln	Arg	Thr	Arg	Arg	Arg	Thr	Pro	Arg	Pro	Gly
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Glu	Gln	Val	Pro	Pro	Val	Pro	Ser	Pro	Gln	Asp	Leu	Leu	Leu	Val	Glu

205

His <210> <211> 174 <212> PRT <213> Artificial Sequence <220> G-CSF: 13rd, 83rd, 113rd, 140th, 144th or 160th Phe is replaced <223> by Val. <400> Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln Ser Phe Leu Leu Lys 5 Cys Leu Glu Gln Val Arg Lys Ile Gln Gly Asp Gly Ala Ala Leu Gln 25 Glu Lys Leu Cys Ala Thr Tyr Lys Leu Cys His Pro Glu Glu Leu Val 35 40 Leu Leu Gly His Ser Leu Gly Ile Pro Trp Ala Pro Leu Ser Ser Cys 50 55 Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser Gln Leu His Ser 65 70 75 Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu Glu Gly Ile Ser 85 90 Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu Asp Val Ala Asp 100 105 Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu Leu Gly Met Ala Pro 115 120 125

200

195

Ala	Leu 130		Pro	Thr	Gln	Gly 135		Met	Pro	Ala	Phe		Ser	Ala	a Phe	
Gln	Arg	Arg	Ala	Gly	Gly	Val	Leu	Val	Ala	Ser	His	Leu	Gln	Ser	Phe	
145					150					155					160	
Leu	Glu	Val	Ser	Tyr	Arg	Val	Leu	Arg	His	Leu	Ala	Gln	Pro			
				165					170							
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<21	3>	Ar	tifi	cial	Seq	uenc	е									
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<22	3>	GM	-CSF	47	th,	103r	d, 10	06th	, 113	3rd o	or 1	19th	Phe	is	replaced	рÀ
		Va.	1.													
<40	1	5														
			_	C	Dro	Sar	Pro	S ~ ~	mp ~		_	_	<b>61</b>	•		
лта															11 - 1	
1		ліа	Arg		FIO	361	110	001		GIN	Pro	Trp	GIU		Val	
1		ALG	Arg	Ser 5	FIO	361	110	202	10	GIN	Pro	Trp	GIU	H15	Val	
				5					10					15		
			Gln	5				Leu	10				Arg	15		
			Gln	5					10					15		
Asn	Ala	Ile	Gln 20	5 Glu	Ala	Arg	Arg	Leu 25	10 Leu	Asn	Leu	Ser	Arg 30	15 Asp	Thr	
Asn	Ala	Ile	Gln	5 Glu	Ala	Arg	Arg	Leu 25	10 Leu	Asn	Leu	Ser Glu	Arg 30	15 Asp	Thr	
Asn	Ala	Ile Glu	Gln 20	5 Glu	Ala	Arg	Arg Val	Leu 25	10 Leu	Asn	Leu	Ser	Arg 30	15 Asp	Thr	
Asn Ala	Ala Ala	Ile Glu 35	Gln 20 Met	5 Glu Asn	Ala Glu	Arg Thr	Arg Val 40	Leu 25 Glu	10 Leu Val	Asn · Ile	Leu Ser	Ser Glu 45	Arg 30 Met	15 Asp Phe	Thr Asp	
Asn Ala	Ala Ala	Ile Glu 35	Gln 20	5 Glu Asn	Ala Glu	Arg Thr	Arg Val 40	Leu 25 Glu	10 Leu Val	Asn · Ile	Leu Ser	Ser Glu 45	Arg 30 Met	15 Asp Phe	Thr Asp	
Asn Ala	Ala Ala Gln	Ile Glu 35	Gln 20 Met	5 Glu Asn	Ala Glu	Arg Thr Leu	Arg Val 40	Leu 25 Glu	10 Leu Val	Asn · Ile	Leu Ser Glu	Ser Glu 45	Arg 30 Met	15 Asp Phe	Thr Asp	
Asn Ala Leu	Ala Ala Gln 50	Ile Glu 35 Glu	Gln 20 Met	5 Glu Asn Thr	Ala Glu Cys	Arg Thr Leu 55	Arg Val 40 Gln	Leu 25 Glu Thr	10 Leu Val Arg	Asn Ile Leu	Leu Ser Glu 60	Ser Glu 45 Leu	Arg 30 Met Tyr	15 Asp Phe Lys	Thr Asp Gln	
Asn Ala Leu	Ala Ala Gln 50	Ile Glu 35 Glu	Gln 20 Met	5 Glu Asn Thr	Ala Glu Cys	Arg Thr Leu 55	Arg Val 40 Gln	Leu 25 Glu Thr	10 Leu Val Arg	Asn Ile Leu	Leu Ser Glu 60	Ser Glu 45 Leu	Arg 30 Met Tyr	15 Asp Phe Lys	Thr Asp Gln	
Asn Ala Leu	Ala Ala Gln 50 Leu	Ile Glu 35 Glu	Gln 20 Met	5 Glu Asn Thr	Ala Glu Cys Leu	Arg Thr Leu 55	Arg Val 40 Gln	Leu 25 Glu Thr	10 Leu Val Arg	Asn Ile Leu	Leu Ser Glu 60	Ser Glu 45 Leu	Arg 30 Met Tyr	15 Asp Phe Lys	Thr Asp Gln Met	
Asn Ala Leu Gly 65	Ala Ala Gln 50 Leu	Ile Glu 35 Glu Arg	Gln 20 Met	5 Glu Asn Thr	Ala Glu Cys Leu 70	Arg Thr Leu 55	Arg Val 40 Gln	Leu 25 Glu Thr	10 Leu Val Arg	Asn Ile Leu Gly 75	Leu Ser Glu 60	Ser Glu 45 Leu	Arg 30 Met Tyr	15 Asp Phe Lys Met	Thr Asp Gln Met 80	
Asn Ala Leu Gly 65	Ala Ala Gln 50 Leu	Ile Glu 35 Glu Arg	Gln 20 Met Pro	5 Glu Asn Thr	Ala Glu Cys Leu 70	Arg Thr Leu 55	Arg Val 40 Gln	Leu 25 Glu Thr	10 Leu Val Arg	Asn Ile Leu Gly 75	Leu Ser Glu 60	Ser Glu 45 Leu	Arg 30 Met Tyr	15 Asp Phe Lys Met	Thr Asp Gln Met 80	

100 105 Phe Leu Leu Val Ile Pro Phe Asp Cys Trp Glu Pro Val Gln Glu 120 <210> <211> 191 <212> PRT <213> Artificial Sequence <220> GH: 1st, 10th, 25th, 31st, 44th, 54th, 92th, 97th, 139th, 146th, <223> 166th, 176th or 191st Phe is replaced by Val. <400> Phe Pro Thr Ile Pro Leu Ser Arg Leu Phe Asp Asn Ala Met Leu Arg 5 10 1 Ala His Arg Leu His Gln Leu Ala Phe Asp Thr Tyr Gln Glu Phe Glu 25 20 Glu Ala Tyr Ile Pro Lys Glu Gln Lys Tyr Ser Phe Leu Gln Asn Pro 35 40 Gln Thr Ser Leu Cys Phe Ser Glu Ser Ile Pro Thr Pro Ser Asn Arg 60 50 55 Glu Glu Thr Gln Gln Lys Ser Asn Leu Glu Leu Leu Arg Ile Ser Leu 75 70 65 Leu Leu Ile Gln Ser Trp Leu Glu Pro Val Gln Phe Leu Arg Ser Val 95 90 85 Phe Ala Asn Ser Leu Val Tyr Gly Ala Ser Asp Ser Asn Val Tyr Asp 105 110

100

Ala Thr Gln Ile Ile Thr Phe Glu Ser Phe Lys Glu Asn Leu Lys Asp

Leu Leu Lys Asp Leu Glu Glu Gly Ile Gln Thr Leu Met Gly Arg Leu 120 115 Glu Asp Gly Ser Pro Arg Thr Gly Gln Ile Phe Lys Gln Thr Tyr Ser 135 130 Lys Phe Asp Thr Asn Ser His Asn Asp Asp Ala Leu Leu Lys Asn Tyr 150 155 145 Gly Leu Leu Tyr Cys Phe Arg Lys Asp Met Asp Lys Val Glu Thr Phe 165 170 Leu Arg Ile Val Gln Cys Arg Ser Val Glu Gly Ser Cys Gly Phe 190 185 180 <210> <211> 165 <212> PRT Artificial Sequence <213> <220> IFN-alpha 2A: 27th, 36th, 38th, 43rd, 47th, 64th, 67th, 84th, <223> 123rd or 151st Phe is replaced by Val. <400> Cys Asp Leu Pro Gln Thr His Ser Leu Gly Ser Arg Arg Thr Leu Met Leu Leu Ala Gln Met Arg Lys Ile Ser Leu Phe Ser Cys Leu Lys Asp 20 25 Arg His Asp Phe Gly Phe Pro Gln Glu Glu Phe Gly Asn Gln Phe Gln 40 35 Lys Ala Glu Thr Ile Pro Val Leu His Glu Met Ile Gln Gln Ile Phe

	50					55					60					
Asn 65	Leu	Phe	Ser	Thr	Lys 70	Asp	Ser	Ser	Ala	Ala 75	Trp	Asp	Glu	Thr	Leu 80	
Leu	Asp	Lys	Phe	Tyr 85	Thr	Glu	Leu	Tyr	Gln 90	Gln	Leu	Asn	Asp	Leu 95	Glu	
Ala	Cys	Val	Ile 100	Gln	Gly	Val	Gly	Val 105	Thr	Glu	Thr	Pro	Leu 110	Met	Lys	
Glu	Asp	Ser 115	Ile	Leu	Ala	Val	Arg 120	Lys	Tyr	Phe	Gln	Arg 125	Ile	Thr	Leu	
Туг	Leu 130	Lys	Glu	Lys	Lys	Tyr 135	Ser	Pro	Cys	Ala	Trp	Glu	Val	Val	Arg	
Ala 145	Glu	Ile	Met	Arg	Ser 150	Phe	Ser	Leu	Ser	Thr 155	Asn	Leu	Gln	Glu	Ser 160	
Leu	Arg	Ser	Lys	Glu 165												
<210	0>	8						-								
<21	<b>L&gt;</b>	165	5													
<212	2>	PR'	r													
<213	3>	Art	cific	cial	Sequ	uence	е									
<220	)>															
<223	3>				2B: 2 51st						_	47th	, 641	th,	67th,	84th
<400	)>	8														
		Leu	Pro	Gln 5	Thr	His	Ser	Leu	Gly 10	Ser	Arg	Arg	Thr	Leu 15	Met	•
Leu	Leu	Ala	Gln 20	Met	Arg	Arg	Ile	Ser 25	Leu	Phe	Ser	Cys	Leu 30	Lys	Asp	

Arg His Asp Phe Gly Phe Pro Gln Glu Glu Phe Gly Asn Gln Phe Gln 35 Lys Ala Glu Thr Ile Pro Val Leu His Glu Met Ile Gln Gln Ile Phe 55 50 Asn Leu Phe Ser Thr Lys Asp Ser Ser Ala Ala Trp Asp Glu Thr Leu 70 65 Leu Asp Lys Phe Tyr Thr Glu Leu Tyr Gln Gln Leu Asn Asp Leu Glu 90 85 Ala Cys Val Ile Gln Gly Val Gly Val Thr Glu Thr Pro Leu Met Lys 105 100 Glu Asp Ser Ile Leu Ala Val Arg Lys Tyr Phe Gln Arg Ile Thr Leu 120 115 Tyr Leu Lys Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val Arg 135 130 Ala Glu Ile Met Arg Ser Phe Ser Leu Ser Thr Asn Leu Gln Glu Ser 160 . 150 155 Leu Arg Ser Lys Glu 165 <210> <211> 166 PRT <212> <213> Artificial Sequence <220> IFN-Beta: 8th, 38th, 50th, 67th, 70th, 111st or 154th Phe is <223> replaced by Val. <400>

Met 1	Ser	Tyr	Asn	Leu 5	Leu	Gly	Phe	Leu	Gln 10	Arg	Ser	Ser	Asn	Cys 15	Gln
	Gln	Lys	Leu	Leu	Trp	Gln	Leu	Asn	Gly	Arg	Leu	Glu	Tyr	Cys	Leu
			20					25					30		
Lys	Asp	Arg 35	Arg	Asn	Phe	Asp	Ile 40	Pro	Glu	Glu	Ile	Lys 45	Gln	Leu	Gln
Gln	Phe 50	Gln	Lys	Glu	Asp	Ala 55	Ala	Val	Thr	Ile	Tyr 60	Glu	Met	Leu	Gln
Asn 65	Ile	Phe	Ala	Ile	Phe 70	Arg	Gln	Asp	Ser	Ser 75	Ser	Thr	Gly	Trp	Asn 80
Glu	Thr	Ile	Val	Glu 85	Asn	Leu	Leu	Ala	Asn 90	Val	Tyr	His	Gln	Arg 95	Asn
His	Leu	Lys	Thr 100	Val	Leu	Glu	Glu	Lys 105	Leu	Glu	Lys	Glu	Asp 110	Phe	Thr
Arg	Gly	Lys 115	Arg	Met.	Ser	Ser	Leu 120	His	Leu	Lys	Arg	Tyr 125	Tyr	Gly	Arg
Ile	Leu 130	His	Tyr	Leu	Lys	Ala 135	Lys	Glu	Asp	Ser	His 140	Cys	Ala	Trp	Thr
Ile 145		Arg	Val	Glu	Ile 150	Leu	Arg	Asn	Phe	Tyr 155	Val	Ile	Asn	Arg	Leu 160
Thr	Gly	Tyr	Leu	Arg 165											
<21	0>	10													
<21	1>	14	6												
<21	2>	PR'	Т												
<21	3>	Ar	tifi	cial	Seq	uenc	е								
<22	0>														

IFN-gamma: 18th, 32nd, 55th, 57th, 60th, 63rd, 84th, 85th, 95th

<223>

or 139th Phe is replaced by Val. <400> 10 Cys Tyr Cys Gln Asp Pro Tyr Val Lys Glu Ala Glu Asn Leu Lys Lys 5 Tyr Phe Asn Ala Gly His Ser Asp Val Ala Asp Asn Gly Thr Leu Phe 25 20 Leu Gly Ile Leu Lys Asn Trp Lys Glu Glu Ser Asp Arg Lys Ile Met 45 35 40 Gln Ser Gln Ile Val Ser Phe Tyr Phe Lys Leu Phe Lys Asn Phe Lys 50 55 60 Asp Asp Gln Ser Ile Gln Lys Ser Val Glu Thr Ile Lys Glu Asp Met 70 75 Asn Val Lys Phe Phe Asn Ser Asn Lys Lys Lys Arg Asp Asp Phe Glu 90 Lys Leu Thr Asn Tyr Ser Val Thr Asp Leu Asn Val Gln Arg Lys Ala 100 105 110 Ile His Glu Leu Ile Gln Val Met Ala Glu Leu Ser Pro Ala Ala Lys 125 120 115 Thr Gly Lys Arg Lys Arg Ser Gln Met Leu Phe Gln Gly Arg Arg Ala 140 135 130 Ser Gln 145 <210> 11 <211> 172 <212> PRT Artificial Sequence <213>

<223	<b>5</b> >	117	-ome	ega:	2/11	1, 5	CII,	20 61	1, 0	) C11,	0011	1, 12	. 4 C11	OL .	
		rep	olace	ed by	y Val	۱.									
<400		11									•				
Cys 1	Asp	Leu	Pro	Gln 5	Asn	His	Gly	Leu	Leu 10	Ser	Arg	Asn	Thr	Leu 15	Val
Leu	Leu	His	Gln 20	Met	Arg	Arg	Ile	Ser 25	Pro	Phe	Leu	Cys	Leu 30	Lys	Asp
Arg	Arg	Asp 35	Phe	Arg	Phe	Pro	Gln 40	Glu	Met	Val	Lys	Gly 45	Ser	Gln	Leu
Gln	Lys 50	Ala	His	Val	Met	Ser 55	Val	Leu	His	Glu	Met 60	Leu	Gln	Gln	Ile
Phe 65	Ser	Leu	Phe	His	Thr 70	Glu	Arg	Ser	Ser	Ala 75	Ala	Trp	Asn	Met	Thr 80
Leu	Leu	Asp	Gln	Leu 85	His	Thr	Gly	Leu	His 90	Gln	Gln	Leu	Gln	His 95	Leu
Glu	Thr	Cys	Leu 100	Leu	Gln	Val	Val	Gly 105	Glu	Gly	Glu	Ser	Ala 110	Gly	Ala
Ile	Ser	Ser 115	Pro	Ala	Leu	Thr	Leu 120	Arg	Arg	Tyr	Phe	Gln 125	Gly	Ile	Arg
Val	Туг 130	Leu	Lys	Glu	Lys	Lys 135	Tyr	Ser	Asp	Cys	Ala 140	Trp	Glu	Val	Val
Arg 145	Met	Glu	Ile	Met	Lys 150	Ser	Leu	Phe	Leu	Ser 155	Thr	Asn	Met	Gln	Glu 160
Arg	Leu	Arg	Ser	Lys 165	Asp	Arg	Asp	Leu	Gly 170	Ser	Ser				

<220>

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		or	183	rd Pł	ne is	s rep	olace	ed by	y Val	L.			٠			
<400	)>	12														
Leu	Asp	Leu	Lys	Leu	Ile	Ile	Phe	Gln	Gln	Arg	Gln	Val	Asn	Gln	Glu	
1				5					10					15		
Ser	Leu	Lys	Leu 20	Leu	Asn	Lys	Leu	Gln 25	Thr	Leu	Ser	Ile	Gln 30	Gln	Cys	
Leu	Pro	His 35	Arg	Lys	Asn	Phe	Leu 40	Leu	Pro	Gln	Lys	Ser 45	Leu	Ser	Pro	
Gln	Gln 50	Tyr	Gln	Lys	Gly	His 55	Thr	Leu	Ala	Ile	Leu 60	His	Glu	Met	Leu	
Gln	Gln	Ile	Phe	Ser	Leu	Phe	Arg	Ala	Asn	Ile	Ser	Leu	Asp	Gly	Trp	
65					70					75					80	
Glu	Glu	Asn	His	Thr 85	Glu	Lys	Phe	Leu	Ile 90	Gln	Leu	His	Gln	Gln 95	Leu	
Glu	Tyr	Leu	Glu 100	Ala	Leu	Met	Gly	Leu 105	Glu	Ala	Glu	Lys	Leu 110	Ser	Gly	
Thr	Leu	Gly 115	Ser	Asp	Asn	Leu	Arg 120	Leu	Gln	Val	Lys	Met 125	Tyr	Phe	Arg	
Arg	Ile 130	His	Asp	Tyr	Leu	Glu 135	Asn	Gln	Asp	Tyr	Ser 140	Thr	Cys	Ala	Trp	
71-	T1 -	17- 3	C1-	17 n 1	C1	T1.	C ~ ~	7 ~~	Cus	Ton	Pho	Pho	V = 1	Dhe	Sar	

155

160

145 Leu Thr Glu Lys Leu Ser Lys Gln Gly Arg Pro Leu Asn Asp Met Lys 170 165 Gln Glu Leu Thr Thr Glu Phe Arg Ser Pro Arg 180 185 <210> 13 133 <211> <212> PRT <213> Artificial Sequence <220> IL-2: 42nd, 44th, 78th, 103rd, 117th or 124th Phe is replaced by <223> Val. <400> 13 Ala Pro Thr Ser Ser Ser Thr Lys Lys Thr Gln Leu Gln Leu Glu His 10 5 Leu Leu Leu Asp Leu Gln Met Ile Leu Asn Gly Ile Asn Asn Tyr Lys 20 2.5 30 Asn Pro Lys Leu Thr Arg Met Leu Thr Phe Lys Phe Tyr Met Pro Lys 45 40 35 Lys Ala Thr Glu Leu Lys His Leu Gln Cys Leu Glu Glu Glu Leu Lys 60 55 50 Pro Leu Glu Glu Val Leu Asn Leu Ala Gln Ser Lys Asn Phe His Leu 70 75 Arg Pro Arg Asp Leu Ile Ser Asn Ile Asn Val Ile Val Leu Glu Leu 90 95 85 Lys Gly Ser Glu Thr Thr Phe Met Cys Glu Tyr Ala Asp Glu Thr Ala 105 110 100

150

Thr Ile Val Glu Phe Leu Asn Arg Trp Ile Thr Phe Cys Gln Ser Ile 125 120 115 Ile Ser Thr Leu Thr 130 <210> 14 <211> 133 <212> PRT <213> Artificial Sequence <220> IL-3: 37th, 61st, 107th, 113rd or 133rd Phe is replaced by Val. <223> <400> 14 Ala Pro Met Thr Gln Thr Thr Pro Leu Lys Thr Ser Trp Val Asn Cys Ser Asn Met Ile Asp Glu Ile Ile Thr His Leu Lys Gln Pro Pro Leu Pro Leu Leu Asp Phe Asn Asn Leu Asn Gly Glu Asp Gln Asp Ile Leu Met Glu Asn Asn Leu Arg Arg Pro Asn Leu Glu Ala Phe Asn Arg Ala Val Lys Ser Leu Gln Asn Ala Ser Ala Ile Glu Ser Ile Leu Lys Asn Leu Leu Pro Cys Leu Pro Leu Ala Thr Ala Ala Pro Thr Arg His Pro Ile His Ile Lys Asp Gly Asp Trp Asn Glu Phe Arg Arg Lys Leu Thr Phe Tyr Leu Lys Thr Leu Glu Asn Ala Gln Ala Gln Gln Thr Thr Leu

Ser	Leu	Ala	Ile	Phe												
	130															
<210	)>	15														
<21	1>	12	9													
<212	2>	PR!	Г									•				
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<223	3>			33rd	, 45 <sup>.</sup>	th,	55th	, 73:	rd,	82nd	or	112n	d Ph	e is	replaced	рy
		Va.	1.													
	_															
<400		15		-1-	<b>m</b> 1	<b>.</b>	<b>61</b> -	<b>63</b>	<b>-1</b> -	T1 -	<b>T</b>	m>	Ŧ	7	0	
	гуs	Cys	Asp		Thr	ьeu	GIN	GIU		Ile	гуѕ	Thr	Leu		Ser	
1				5					10					15		
	Th ×	C1.,	Cln	Lve	ሞኮሎ	Len	CVE	Thr	Glu	Leu	<b>ም</b> ኮ ድ	V=1	Thr	Asn	Tle	
ьеu	1111	GIU	20	пуз	1111	пец	Cys	25	Giu	neu	1111	Val	30	лэр	110	
			20					23				•				
Phe	Ala	Ala	Ser	Lvs	Asn	Thr	Thr	Glu	Lvs	Glu	Thr	Phe	Cvs	Arq	Ala	
		35		_3 -			40		•			45	-	_		
Ala	Thr	Val	Leu	Arg	Gln	Phe	Tyr	Ser	His	His	Glu	Lys	Asp	Thr	Arg	
	50					55					60					
Cys	Leu	Gly	Ala	Thr	Ala	Gln	Gln	Phe	His	Arg	His	Lys	Gln	Leu	Ile	
65					70					75					80	
Arg	Phe	Leu	Lys	Arg	Leu	Asp	Arg	Asn	Leu	Trp	Gly	Leu	Ala	Gly	Leu	
				85					90					95	•	
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Lys	Met	Ala	Glu	Lys	Asp	Gly	Cys	Phe	Gln	Ser	Gly	Phe	Asn	Glu	Glu	
65					70					75					. 80	
Thr	Cys	Leu	Val	Lys	Ile	Ile	Thr	Gly	Leu	Leu	Glu	Phe	Glu	Val	Tyr	
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Leu	Glu	Tyr	Leu	Gln	Asn	Arg	Phe	Glu	Ser	Ser	Glu	Glu	Gln	Ala	Arg	
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Ala	Val	Gln	Met	Ser	Thr	Lys	Val	Leu	Ile	Gln	Phe		Gln	Lys	Lys	
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Ala	Lys	Asn	Leu	Asp	Ala		Thr	Thr	Pro	Asp		Thr	Thr	Asn	Ala	
	130					135					140					
_				_	_			۵.	_	63	m.	<b>.</b>	63 =	20.00	Wa t	
	Leu	Leu	Thr	Lys		Gln	Ala	Gin	Asn		Trp	Leu	GIN	ASP		
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Gln Val Glu Phe Lys Thr Met Asn Ala Lys Leu Leu Met Asp Pro Lys 120 Arq Gln Ile Phe Leu Asp Gln Asn Met Leu Ala Val Ile Asp Glu Leu Met Gln Ala Leu Asn Phe Asn Ser Glu Thr Val Pro Gln Lys Ser Ser 150 Leu Glu Glu Pro Asp Phe Tyr Lys Thr Lys Ile Lys Leu Cys Ile Leu 165 170 Leu His Ala Phe Arg Ile Arg Ala Val Thr Ile Asp Arg Val Met Ser 185 Tyr Leu Asn Ala Ser 195 <210> 19 <211> 146 PRT <212> Artificial Sequence <213> <220> LPT: 41st or 92nd Phe is replaced by Val. <223> <400> 19 Val Pro Ile Gln Lys Val Gln Asp Asp Thr Lys Thr Leu Ile Lys Thr 1 5 Ile Val Thr Arg Ile Asn Asp Ile Ser His Thr Gln Ser Val Ser Ser 25 20 Lys Gln Lys Val Thr Gly Leu Asp Phe Ile Pro Gly Leu His Pro Ile 40 35 Leu Thr Leu Ser Lys Met Asp Gln Thr Leu Ala Val Tyr Gln Gln Ile 50 55

Leu Thr Ser Met Pro Ser Arg Asn Val Ile Gln Ile Ser Asn Asp Leu 70 65 Glu Asn Leu Arg Asp Leu Leu His Val Leu Ala Phe Ser Lys Ser Cys 85 90 His Leu Pro Trp Ala Ser Gly Leu Glu Thr Leu Asp Ser Leu Gly Gly 105 100 Val Leu Glu Ala Ser Gly Tyr Ser Thr Glu Val Val Ala Leu Ser Arg 115 120 125 Leu Gln Gly Ser Leu Gln Asp Met Leu Trp Gln Leu Asp Leu Ser Pro 135 140 Gly Cys 145 <210> 20 <211> 180 <212> PRT Artificial Sequence <220> LIF: 41st, 52nd, 67th, 70th, 156th or 180th Phe is replaced by Val. Ser Pro Leu Pro Ile Thr Pro Val Asn Ala Thr Cys Ala Ile Arg His 15 5 Pro Cys His Asn Asn Leu Met Asn Gln Ile Arg Ser Gln Leu Ala Gln 20 Leu Asn Gly Ser Ala Asn Ala Leu Phe Ile Leu Tyr Tyr Thr Ala Gln 35 40 45

Gly Glu Pro Phe Pro Asn Asn Leu Asp Lys Leu Cys Gly Pro Asn Val 55 50 Thr Asp Phe Pro Pro Phe His Ala Asn Gly Thr Glu Lys Ala Lys Leu 75 70 Val Glu Leu Tyr Arg Ile Val Val Tyr Leu Gly Thr Ser Leu Gly Asn Ile Thr Arg Asp Gln Lys Ile Leu Asn Pro Ser Ala Leu Ser Leu His 100 105 Ser Lys Leu Asn Ala Thr Ala Asp Ile Leu Arg Gly Leu Leu Ser Asn 120 115 Val Leu Cys Arg Leu Cys Ser Lys Tyr His Val Gly His Val Asp Val 135 Thr Tyr Gly Pro Asp Thr Ser Gly Lys Asp Val Phe Gln Lys Lys 150 155 Leu Gly Cys Gln Leu Leu Gly Lys Tyr Lys Gln Ile Ile Ala Val Leu 165 170 Ala Gln Ala Phe 180 <210> 21 <211> 522 <212> PRT <213> Artificial Sequence <220> M-CSF: 35th, 37th, 54th, 67th, 91st, 106th, 121st, 135th, 143rd, <223> 229th, 255th, 311st, 439th, 466th or 485th Phe is replaced by Val. <400>

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Met 65	Arg	Phe	Arg	Asp	Asn 70	Thr	Pro	Asn	Ala	Ile 75	Ala	Ile	Val	Gln	Lev 80
Gln	Glu	Leu	Ser	Leu 85	Arg	Leu	Lys	Ser	Cys 90	Phe	Thr	Lys	Asp	Tyr 95	Glu
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Leu	Leu	Glu 115	Lys	Val	Lys	Asn	Val 120	Phe	Asn	Glu	Thr	Lys 125	Asn	Leu	Leu
Asp	Lys 130	Asp	Trp	Asn	Ile		Ser	Lys	Asn	Cys	Asn 140	Asn	Ser	Phe	Ala
Glu 145	Cys	Ser	Ser	Gln	Asp 150	Val	Val	Thr	Lys	Pro 155	Asp	Cys	Asn	Cys	Leu 160
Tyr	Pro	Lys	Ala	Ile 165	Pro	Ser	Ser	Asp	Pro 170	Ala	Ser	Val	Ser	Pro 175	His
Gln	Pro	Leu	Ala 180	Pro	Ser	Met	Ala	Pro 185	Val	Ala	Gly	Leu	Thr 190	Trp	Glu
Asp	Ser	Glu 195	Gly	Thr	Glu	Gly	Ser 200	Ser	Leu	Leu	Pro	Gly 205	Glu	Gln	Pro
Leu	His	Thr	Val	Asp	Pro	Gly	Ser	Ala	Lys	Gln	Arg	Pro	Pro	Arg	Ser

Glu Glu Val Ser Glu Tyr Cys Ser His Met Ile Gly Ser Gly His Leu

Gln Ser Leu Gln Arg Leu Ile Asp Ser Gln Met Glu Thr Ser Cys Gln

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Thr 225	Cys	Gln	Ser	Phe	Glu 230	Pro	Pro	Glu	Thr	Pro 235	Val	Val	Lys	Asp	Ser 240
Thr	Ile	Gly	Gly	Ser 245	Pro	Gln	Pro	Arg	Pro 250	Ser	Val	Gly	Ala	Phe 255	Asn
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Pro	Glu	Glu 275	Ala	Ser	Gly	Glu	Ala 280	Ser	Glu	Ile	Pro	Val 285	Pro	Gln	Gly
Thr	Glu 290	Leu	Ser	Pro	Ser	Arg 295	Pro	Gly	Gly	Gly	Ser 300	Met	Gln	Thr	Glu
Pro 305	Ala	Arg	Pro	Ser	Asn 310	Phe	Leu	Ser	Ala	Ser 315	Ser	Pro	Leu	Pro	Ala 320
Ser	Ala	Lys	Gly	Gln 325	Gln	Pro	Ala	Asp	Val (330	Thr	Gly	Thr	Ala	Leu 335	Pro
Arg	Val	Gly	Pro 340	Val	Arg	Pro	Thr	Gly 345	Gln	Asp	Trp	Asn	His 350	Thr	Pro
Gln	Lys	Thr 355	Asp	His	Pro	Ser	Ala 360	Leu	Leu	Arg	Asp	Pro 365	Pro	Glu	Pro
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Ser 385	Thr	Leu	Ser	Ala	Gln 390	Pro	Gln	Leu	Ser	Arg 395	Ser	His	Ser	Ser	Gly 400
Ser	Val	Leu	Pro	Leu 405	Gly	Glu	Leu	Glu	Gly 410	Arg	Arg	Ser	Thr	Arg 415	Asp
Arg	Arg	Ser	Pro 420	Ala	Glu	Pro	Glu	Gly 425	Gly	Pro	Ala	Ser	Glu 430	Gly	Ala

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His	Glu 450	Arg	Gln	Ser	Glu	Gly 455	Ser	Ser	Ser	Pro	Gln 460	Leu	Gln	Glu	Ser
Val 465	Phe	His	Leu	Leu	Val 470	Pro	Ser	Val	Ile	Leu 475	Val	Leu	Leu	Ala	Val 480
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Leu	Gln	Lys	Gln 20	Thr	Asp	Leu	Met	Gln 25	Asp	Thr	Ser	Arg	Leu 30	Leu	Asp
Pro	Tyr	Ile 35	Arg	Ile	Gln	Gly	Leu 40	Asp	Val	Pro	Lys	Leu 45	Arg	Glu	His

Cys Arg Glu Arg Pro Gly Ala Phe Pro Ser Glu Glu Thr Leu Arg Gly 50 55 Leu Gly Arg Arg Gly Phe Leu Gln Thr Leu Asn Ala Thr Leu Gly Cys 70 Val Leu His Arg Leu Ala Asp Leu Glu Gln Arg Leu Pro Lys Ala Gln Asp Leu Glu Arg Ser Gly Leu Asn Ile Glu Asp Leu Glu Lys Leu Gln 105 Met Ala Arg Pro Asn Ile Leu Gly Leu Arg Asn Asn Ile Tyr Cys Met 115 120 Ala Gln Leu Leu Asp Asn Ser Asp Thr Ala Glu Pro Thr Lys Ala Gly 135 Arg Gly Ala Ser Gln Pro Pro Thr Pro Thr Pro Ala Ser Asp Ala Phe 150 155 Gln Arg Lys Leu Glu Gly Cys Arg Phe Leu His Gly Tyr His Arg Phe 165 170 Met His Ser Val Gly Arg Val Phe Ser Lys Trp Gly Glu Ser Pro Asn 180 185 Arg Ser Arg Arg His Ser Pro His Gln Ala Leu Arg Lys Gly Val Arg 195 200 Arg Thr Arg Pro Ser Arg Lys Gly Lys Arg Leu Met Thr Arg Gly Gln 215 220 Leu Pro Arg 225 <210> 23 <211> 191 <212> PRT

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Glu	Thr	Туr 35		Pro	Lys	Asp	Gln 40	Lys	Tyr	Ser	Phe	Leu 45	His	Asp	Ser	
Gln	Thr 50	Ser	Phe	Cys	Phe	Ser 55	Asp	Ser	Ile	Pro	Thr 60	Pro	Ser	Asn	Met	
Glu 65	Glu	Thr		Gln	Lys 70				Glu				Ile	Ser	Leu 80	
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Phe	Ala	Asn	Asn 100	Leu	Val	Tyr	Asp	Thr 105	Ser	Asp	Ser	Asp	Asp 110	Tyr	His	٠
Leu	Leu	Lys 115	Asp	Leu	Glu	Glu	Gly 120	Ile	Gln	Thr	Leu	Met 125	Gly	Arg	Leu	
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Lys 145	Phe	Asp	Thr		Ser 150	His	Asn	His	Asp	Ala 155	Leu	Leu	Lys	Asn	Tyr 160	
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Glu Glu Phe Phe Arg Ile Phe Asn Arg Ser Ile Asp Ala Phe Lys Asp

Leu Arg Met Val Gln Cys Arg Ser Val Glu Gly Ser Cys Gly Phe

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Ser 145	Pro	Glu	Lys	Asp	Ser 150	Arg	Val	Ser	Val	Thr 155	Lys	Pro	Phe	Met	Leu 160		
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Leu	Gly	Pro	Thr	Cys 85	Leu	Ser	Ser	Leu	Leu 90	Gly	Gln	Leu	Ser	Gly 95	Gln
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Val	Pro	Ser	Arg	Thr 165	Ser	Leu	Val	Leu	Thr 170	Leu	Asn	Glu	Leu	Pro 175	Asn
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Thr	Gly	Ser 195	Gly	Leu	Leu	Lys	Trp 200	Gln	Gln	Gly	Phe .	Arg 205	Ala	Lys	Ile
Pro	Gly 210	Leu	Leu	Asn	Gln	Thr 215	Ser	Arg	Ser	Leu	Asp 220	Gln	Ile	Pro	Gly

Tyr 225	Leu	Asn	Arg	Ile	His 230	Glu	Leu	Leu	Asn	Gly 235	Thr	Arg	Gly	Leu	Phe 240		
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